LETTERS TO THE EDITOR

Under-diagnosis of female genital *Chlamydia trachomatis* infection

Chlamydia trachomatis is a major causative agent of genital infections.[1] Conventional methods of laboratory diagnosis such as tissue culture, direct antigen detection by ELISA or direct fluorescent antibody test (DFA) have good records of sensitivity and specificity.[2] However, with the availability of gene amplification methods, it becomes apparent that conventional methods under-diagnose *C trachomatis* infections.[3,4] We have undertaken a pilot study to estimate the level of under-diagnosis in high risk female patients and evaluated the factors associated with the failure in conventional methods.

We defined high risk female patients as those who had had recent sexual contact with partners who had non-gonococcal urethritis (NGU); those who were tested positive for *C trachomatis* previously but were not treated or were inadequately treated and those who exhibited signs and symptoms suggestive of *C trachomatis* infection such as irregular bleeding and inflammation of the cervix. A total of 49 patients were prospectively enrolled into this study. After an initial endocervical swab was taken for *Neisseria gonorrhoea* culture, two further endocervical swabs (labelled as first and second according to the order taken), one endourethral swab and a urine specimen were taken for *C trachomatis* diagnosis. The first endocervical swab was tested by ELISA (VIDAS, Biomerieux, France), and if positive was further confirmed by DFA (Microtrak, Syva, UK). If the first endocervical swab was confirmed as positive, a positive report was issued and no further action was taken. If the initial test was negative, then all specimens from that patient were tested by ELISA, DFA and an in-house semi-nested polymerase chain reaction (PCR) that amplified a fragment of *C trachomatis* major outer membrane protein (MOMP) gene.[5] Discrepant results were further investigated by a second in-house PCR test that amplified the plasmid DNA of *C trachomatis*.[6] A patient was said to be truly infected if the combination of specimens had positive results from at least two of the four methods. All procedures were done blind to avoid bias with the more subjective assays.

Of the 49 patients who participated, 16 (32·7%) tested positive by both ELISA and DFA on the first endocervical swab and there was no discrepancy between ELISA and DFA results. Of the 33 that underwent extended testing, eight fulfilled the defined criteria of true positive. Thus, the true prevalence of *C trachomatis* in this selected population was 49·0% (24/49) and the level of under-diagnosis was 33·3% (8/24). Of the eight patients missed by the initial screening test, two were positive by all methods on the second endocervical swabs while the first swabs were positive by PCR only, suggesting that the problems lay with the specimens. One patient had an endourethral swab positive by all methods while the endocervical swabs were positive by PCR only, indicating that the focus of infection was predominantly in the urethra and not the cervix. Five patients had a combination of specimens positive by the two PCR tests only, suggesting that the levels of infection were below the sensitivity limit of conventional tests. There was one positive PCR result on an endocervical swab which cannot be confirmed by any other methods on any other specimens and was thus considered as equivocal. There were no isolated positive ELISA or DFA findings unconfirmable by another method in this series. The distribution of results among the three categories of patients are listed in the table.

Distribution of Chlamydia trachomatis results among the three categories of patients in the study

Patient group	Negative	Initial positive	After extended testing		
			Positive	Equivocal	Total
NGU Contact	20	4	3*	0	27
Positive elsewhere	2	11	4†	0	17
Symptoms and signs	2	1	1	1	5
Total	24	16	8	1	49

*One patient had the second endocervical swab positive by all tests.
†One patient had a previous positive eye swab, one patient had the second endocervical swab positive by all tests and one patient had the endourethral swab positive by all tests.

The number of patients in this pilot study was small, but the results suggest that conventional methods such as ELISA and DFA under-diagnose *C trachomatis* infection in high risk women by up to 30%. It is impossible for routine diagnostic laboratories to undergo the strategy of this study, using multiple tests on multiple samples. However, with the sensitivity of gene amplification methods, they may be the single test of choice to maximise *C trachomatis* diagnosis, which is important to ensure that all infected patients receive treatment and where appropriate, contact tracing. Quality and site of specimens are important as illustrated in this study but the ultra-sensitivity of these gene amplification methods could at least help to overcome some of these problems.

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Controlling chlamydial infection

The Health of the Nation target for the reduction in incidence of gonorrhoea has already been achieved in some areas and thus it has become necessary to explore the possibility of substituting targets for other infections. Smith *et al*[1] in Glasgow showed a 12% chlamydia rate in 197 asymptomatic women attending for cervical cytology. In Trent Region a pilot study has been conducted to determine whether a community based chlamydia screening exercise would be a worthwhile undertaking.

One large group practice in Arnold, Nottingham (suburban and four practices in South Lincolnshire (rural) were recruited. Cervical swabs were taken at the time that women attended for routine cytology sampling. Information was collected on the age of patients, on whether they were involved in a stable relationship, and on whether there was a present or past history indicative of urogenital infection. The swabs were processed locally using ELISA (IDEIA) kits and the results were made available directly to the general practitioners concerned. The protocol stated that patients should be referred to the local genitourinary medicine clinic for contact tracing, testing for other sexually transmissible infections and treatment, with an option for the general practitioner to test for other infections and give treatment in case of clinical need before referral for contact tracing.

Age was the only category which provided useful discriminative information. This confirms the findings of Ramstedt *et al*[2] in Sweden and Hunter Handsfield *et al*[3] in the USA. There was no conscious selection for screening among the younger women but clearly from the numbers and yields involved there is an element of self-selection (table).

Fortunately it is not necessary to understand this process in order to conclude which age groups satisfy existing criteria of cost effectiveness. However, better definition will be required to evaluate change over time.

Disappointingly, only five out of the 40 positive patients were referred to the local departments of genitourinary medicine. No other patients with positive results were found to have attended the local clinic in the rural area but in contrast the majority of the suburban patients eventually attended. Opportunistic screening and treatment will fail to reduce the prevalence of chlamydia without co-ordinated follow-up and contact tracing.

This study does not tell us whether patients who have once been tested should be retested and if so at what intervals. More importantly we need to develop an initiative which focuses ownership on the medical and nursing staff in general practice, family planning and teenage clinics on whom success finally depends.

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Genitourinary colposcopy services in the UK

I have recently performed a telephone survey of every genitourinary clinic in England, Wales, Scotland and Northern Ireland. My question was a simple one: "do you perform colposcopy in your clinic?"

It would appear from the answers that of 252 genitourinary clinics 93 provide colposcopy services.

Readers can obtain a copy of the address list and contact name if they would care to send me a stamped addressed A4 size envelope.

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Results of cervical swabs

Age group (years)	*Positive/No tested (%)*		
	Surburban	*Rural*	*Total*
15–19	3/17 (17·6)	5/21 (23·8)	8/38 (21·1)
20–24	7/62 (11·3)	5/64 (7·8)	12/126 (9·5)
25–29	3/88 (3·4)	6/74 (8·1)	9/162 (5·6)
30–39	2/179 (4·5)	7/156 (4·5)	9·335 (2·7)
40+	0/99 (0)	2/282 (0·7)	2·381 (0·5)
Total tested	1042	Total Positive	40 (3·8%)